Memorandum

To: Christine Baker, Department of Industrial Relations
Lachlan Taylor, Commission for Health and Safety and Workers' Compensation
Commissioners, Commission for Health and Safety and Workers' Compensation

From: Teryl K. Nuckols, MD, MSHS
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Date: August 30, 2012

Re: Evaluation of Opioid Prescribing Guidelines Using AGREE II*

This memorandum summarizes our additional evaluation of guidelines for the use of opioids to treat pain. Please refer to the previously submitted report for a description of methods used to identify relevant guidelines.

* This work was completed as of August 30, 2012. The author and colleagues plan to submit the work to peer-reviewed medical journals in the future. In preparing the work for submission, methods and results may change slightly from that reported below.

METHODS

Please refer to the previously submitted report, "Identifying Risky Opioid Prescribing Practices," for a description of methods used to identify relevant guidelines. The Figure summarizes our guideline selection process.

After identifying guidelines, we applied several exclusion criteria. We excluded documents that did not meet a commonly used definition of a guideline, "Clinical practice guidelines are statements that include recommendations intended to optimize patient care that are informed by a systematic review of evidence and an assessment of the benefits and harms of alternative care options." Guidelines had to have been published within the past five years because standards of care for opioid treatment are evolving and because guidelines can become out of date within three years. Guidelines had to be published in English.

Because our objective was to evaluate guidelines addressing the use of opioids for pain in general, we excluded guidelines that were limited to specific conditions, populations, types of pain, or settings. This means we excluded documents addressing cancer pain, neuropathic pain, pain at the end of life, post-operative pain, pain associated with labor and delivery, low back pain, carpal tunnel syndrome, osteoarthritis pain, and the use of interventional techniques for pain, etc. Because guidelines addressing acute pain tend to focus on specific conditions or settings, the guidelines in our review generally address chronic pain.

Finally, we sought to evaluate the quality of the guidelines; therefore, we excluded guidelines that did not provide a description of developmental methods and guidelines that were entirely derived from another guideline.

Guideline Quality Assessment

More rigorous development methods should produce higher quality guidelines. To assess guideline quality, we used the Appraisal of Guidelines for Research and Evaluation II (AGREE II), which evaluates several dimensions of guideline development. We also used the AMSTAR, which was designed to assess systematic reviews. Systematic reviews are a fundamental component of the guideline development process and the AMSTAR evaluates them in greater depth than the AGREE II does.

AGREE II

The AGREE II primarily evaluates the process of guideline development, using 23 items across 6 domains. It also includes an outcome assessment whereby appraisers are asked to provide a global rating of the guideline and a recommendation for or against use.

Each item and the global rating are scored on a scale from 1 ("strongly disagree") to 7 ("strongly agree"). Standardized domain scores are determined by aggregating item scores in a domain across all appraisers, and then scaling them as a percentage of the maximum possible score. There is no established minimum score required to distinguish between high and low quality guidelines.

In our evaluation, two to three reviewers appraised the literature reviews described by each guideline, internal medicine physicians trained in health services research and a graduate student in a Masters of Public Health program. The AGREE II Manual recommends that at least 2 appraisers, but preferably 4, rate each guideline. Reviewers discussed ratings to catch errors (e.g., overlooking relevant material within a long guideline); they were not expected to reach agreement.

AMSTAR

AMSTAR has been shown to have good reliability, construct validity, and to be easy to apply.

When scoring the AMSTAR, a "yes" on an individual question receives 1 point, while a "no" or "can't answer" receives no points. For each guideline and question, a summary score equals the number of affirmative responses divided by the number of reviewers (we excluded questions that reviewers agreed were "not applicable"). To create summary scores for each guideline overall, we summed the total number of affirmative responses across all reviewers and divided by the total number of possible affirmative responses (i.e., the number of applicable questions times the number of reviewers).

We used two reviewers per guideline to rate the AMSTAR. Reviewers discussed AMSTAR ratings when there was uncertainty as to whether a question applied to a guideline.

RESULTS

Tables 1 lists the guidelines that met all selection criteria and that were included in the AGREE and AMSTAR evaluations. Tables 2 and 3 list the results of those two evaluations, respectively.

DISCUSSION

This evaluation identified several good quality guidelines that could be considered for potential use in California.

Before delving into the guidelines that may be considered for use, several can be eliminated. These guidelines do address opioid therapy and make useful points about clinical management in certain circumstances. They would not, however, be useful as a general guideline for opioid therapy because they are intended to be used for specific populations, primarily address procedural rather than medical therapies for pain, or address only a very narrow aspect of treating pain. They could, therefore, be considered as supplemental material but not as the main guideline to be used for treating pain. The guidelines that can be eliminated are:

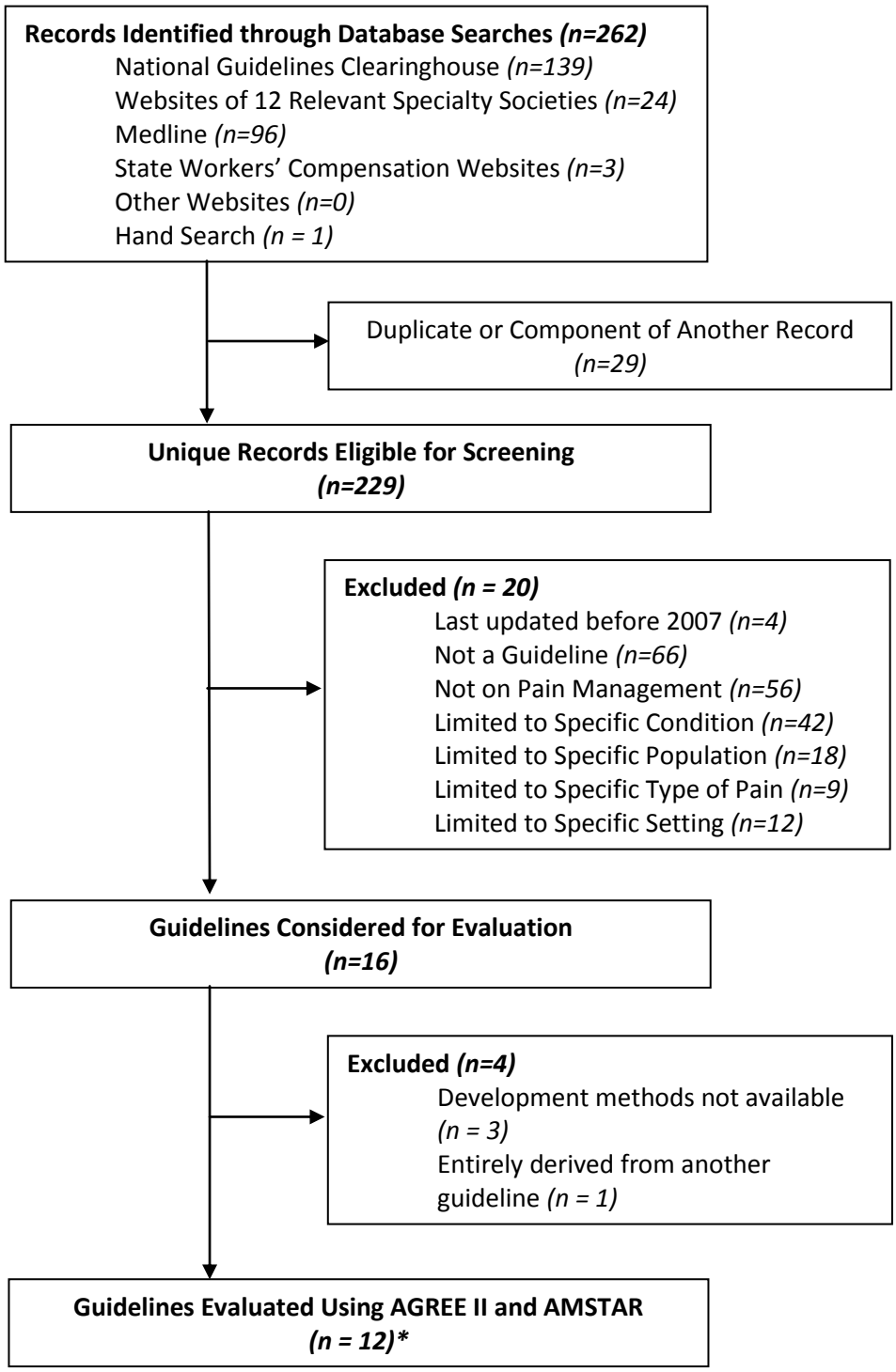
- The American Geriatric Society (AGS) guideline, because it addresses pain management in adults over age 65 (some of whom are remaining in the workforce and for whom the guideline recommends opioids as a first line therapy);
- The American Society of Anesthesiologists (ASA) guideline, because it primarily focuses on procedural modalities used to treat pain;
- The American Society of Interventional Pain Physicians (ASIPP) guideline, because it primarily focuses on procedural modalities used to treat pain; and
- The Fine guideline for opioid rotation, because this is important but only one narrow aspect of using opioids to treat pain.

Of the eight remaining guidelines, we were unable to evaluate the development methods and related aspects of the ODG guideline developed by the Work Loss Data Institute (WLDI) because the content of the guideline was not available. An earlier version of this guideline is currently used in California.

The two guidelines that performed the best in both the AGREE II and the AMSTAR ratings are the guideline by the American Pain Society and the American Academy of Pain Medicine (APS-AAPM), and the Canadian guideline. Thus, these two guidelines may be the most rigorously developed guidelines available on the use of opioids to treat pain. The Institute for Clinical Systems Improvement (ICSI) guideline performed nearly as well on the AGREE II evaluation. The guideline provided limited detail was available on the literature search methods, however. Arguably, the literature search is one of the most important aspects of guideline development. For this reason, the ICSI guideline performed worse on the AMSTAR than on the AGREE II.

Table 3 summarizes how the guidelines performed in addressing key aspects of treatment discussed in our prior report. The three guidelines listed above, APS-AAPM, the Canadian guideline, and ICSI, covered many of the key aspects of treatment.

Figure: Guideline Search and Evaluation Strategy



*The American Geriatric Society updated its guideline in 2009 and stated that the 2002 guideline, which covers slightly different material, was still up to date. When counting guidelines, we considered these to be components of one document.

Table 1. Guidelines Meeting All Inclusion Criteria

Guideline Name	Abbreviated Name	Developer	Last Reviewed
Guidelines for Chronic Use of Opioids	ACOEM	American College of Occupational and Environmental Medicine	2011
Pharmacological Management of Persistent Pain in Older Persons, AGS Panel on Persistent Pain in Older Persons	AGS	American Geriatrics Society	2009
The Management of Persistent Pain in Older Persons, AGS Panel on Persistent Pain in Older Persons, Published in 2002, Reviewed in 2009 and Judged Current	AGS	American Geriatrics Society	2009
Opioid Treatment Guidelines, Clinical guidelines for the Use of Chronic Opioid Therapy in Chronic Noncancer Pain	APS-AAPM	American Pain Society and the American Academy of Pain Medicine	2009
Practice Guidelines for Chronic Pain Management, An Updated Report by the American Society of Anesthesiologists Task Force on Chronic Pain Management and the American Society of Regional Anesthesia and Pain Medicine	ASA	The American Society of Anesthesiologists and the American Society of Regional Anesthesia and Pain Medicine	2010
American Society of Interventional Pain Physicians (ASIPP) Guidelines for Responsible Opioid Prescribing in Chronic Non-Cancer Pain	ASIPP	American Society of Interventional Pain Physicians	2012
Canadian Guideline for Safe and Effective Use of Opioids for Chronic Non-Cancer Pain	Canada	National Opioid Use Guideline Group (NOUGG)	2010
Establishing "Best Practices" for Opioid Rotation: Conclusions of an Expert Panel	Fine	Department of Pain Medicine and Palliative Care, Beth Israel Medical Center and Department of Anesthesiology, Pain Research Center (P.G.F.), University of Utah School of Medicine	2009
Assessment and Management of Chronic Pain	ICSI	Institute for Clinical Systems Improvement	2011
Managing Chronic Non-Terminal Pain in Adults Including Prescribing Controlled Substances	U of M	University of Michigan Health System	2011
Utah Clinical Guidelines on Prescribing Opioids for Treatment of Pain	Utah	Utah Department of Health	2009
VA/DoD Clinical Practice Guideline for Management of Opioid Therapy for Chronic Pain	VA	Department of Defense, Department of Veterans Affairs, and Veterans Health Administration	2010

Pain (Chronic). Guideline from The Official Disability Guidelines product line, including ODG Treatment in Workers Comp, updated annually.	WLDI	Work Loss Data Institute	2011

Table 2. Results: AGREE II Standardized Domain Scores

Domain		Abbreviated Guideline Name											
		ACOEM	**AGS**	**APS-AAPM**	**ASA**	**ASIPP**	**Canada**	**Fine**	**ICSI**	**U of M**	**Utah**	**VA**	**WLDI**
1. Scope and Purpose: The overall aim of the guideline, the specific health questions, and the target population		64%	67%	83%	53%	87%	64%	47%	86%	50%	50%	78%	61%
2. Stakeholder Involvement: The extent to which the guideline was developed by the appropriate stakeholders and represents the views of its intended users		53%	39%	58%	47%	50%	67%	28%	86%	39%	61%	58%	54%
3. Rigor of Development: The process used to gather and synthesize the evidence, the methods to formulate the recommendations, and to update them		46%	49%	77%	32%	60%	69%	29%	65%	26%	39%	49%	51%
4. Clarity of Presentation: The language, structure, and format of the guideline		56%	67%	83%	42%	78%	86%	69%	81%	69%	78%	64%	N/A*
5. Applicability: The likely barriers and facilitators to implementation, strategies to improve uptake, and resource implications of applying the guideline		29%	17%	31%	19%	22%	40%	19%	29%	29%	29%	27%	14%
6. Editorial Independence: The influence of the funding body on development and disclosure of conflicts of interest		67%	71%	96%	4%	64%	58%	42%	79%	46%	46%	17%	36%
Average Overall Quality Score		4.0	4.0	5.5	3.0	5.0	5.5	3.5	5.0	3.5	4.0	4.5	3.7
Recommend Use, Votes, Number	Yes			2		1	1					1	
	Yes, With Modifications		2			2	1		2	1	2	1	
	No	2			2			2		1			
	Total Raters, Number	2	2	2	2	3	2	2	2	2	2	2	N/A

* The guideline is proprietary and text was unavailable so raters could not assess clarity of presentation or decide whether to recommend use. Domains that were rated were based on information the developer has made public about development methods and information related to the other domains.

Table 3. Results: Updated AMSTAR Quality Scores (with multiple reviewers)

AMSTAR Question	Abbreviated Guideline Name											
	ACOEM	AGS	APS-AAPM	ASA	ASIPP	Canada	Fine	ICSI	U of M	Utah	VA	WLDI
1. Was an 'a priori' designed provided?	1/2	2/2	2/2	2/2	2/2	2/2	2/2	2/2	2/2	2/2	2/2	2/2
2. Was there duplicate study selection and data extraction?	0/2	0/2	2/2	0/2	1/2	2/2	0/2	0/2	0/2	0/2	2/2	0/2
3. Was a comprehensive literature search performed?	2/2	1/2	2/2	0/2	0/2	2/2	0/2	1/2	1/2	0/2	2/2	2/2
4. Was the status of publication(ie grey literature) used as an inclusion criterion?	1/2	0/2	1/2	0/2	0/2	0/2	0/2	0/2	1/2	0/2	0/2	1/2
5. Was a list of studies (included and excluded) provided?	0/2	0/2	0/2	0/2	0/2	0/2	0/2	0/2	0/2	0/2	0/2	0/2
6. Were the characteristics of the included studies provided?	0/2	0/2	2/2	0/2	0/2	0/2	0/2	1/2	0/2	0/2	0/2	0/2
7. Was the scientific quality of the included studies assessed and documented?	2/2	2/2	2/2	2/2	1/2	2/2	0/2	2/2	2/2	0/2	2/2	2/2
8. Was the scientific quality of the included studies used appropriately in formulating conclusions?	1/2	2/2	2/2	2/2	2/2	2/2	0/2	1/2	0/2	0/2	2/2	1/2
9. Were the methods used to combine the findings of studies appropriate?	n/a	0/2	0/2	2/2	0/2	1/2	0/2	0/2	0/2	0/2	n/a	0/2
10. Was the likelihood of publication bias assessed?	0/2	0/2	0/2	1/2	0/2	0/2	0/2	0/2	0/2	0/2	0/2	0/2
11. Was the conflict of interest stated?	1/2	0/2	0/2	0/2	0/2	0/2	0/2	0/2	0/2	0/2	0/2	0/2
Points/Total possible points	8/20	7/22	13/22	9/22	6/22	11/22	2/22	7/22	6/22	2/22	10/20	8/22
Overall Summary Score	**40%**	**32%**	**59%**	**41%**	**27%**	**50%**	**9%**	**32%**	**27%**	**9%**	**50%**	**36%**

Table 4: Key Elements of Opioid Treatment

	Abbreviated Guideline Name										
	ACOEM	**AGS**	**APS-AAPM**	**ASA**	**ASIPP**	**Canada**	**Fine**	**ICSI**	**U of M**	**Utah**	**VA**
Reducing the Risk of Opioid Overdose											
1. "High" Daily Dose: Milligrams of Morphine Equivalents per Day	-	-	**200 mg**	-	-	**200 mg**	-	**200 mg**	-	-	-
2. Type of Opioid, Formulation, or Route											
Methadone: Only experienced providers should use, given risk of bioaccumulation and overdose	**√**	**√**	**√**	-	-	**√**	-	**√**	-	**√**	**√**
Fentanyl Patch: Risk of overdose due to variable absorption, risk increased by exercise and exposure to heat; limit to opioid tolerant patients	-	-	-	-	**√**	**√**	-	**√**	-	-	-
Fentanyl Immediate Release: High risk of respiratory suppression, limit to opioid tolerant, safety not established for non-cancer pain, high addiction risk	-	-	-	-	**√**	**√**	-	**√**	-	-	**√**
Meperidine: Bioaccumulation, central nervous system toxicity, seizures	-	-	-	-	-	**√**	-	**√**	-	-	-
3. Titration of Dose: Recommendations for minimizing risks	-	-	**√**	-	-	**√**	-	-	-	-	-
4. Rotation of Medication:											
Equianalgesic dosing tables ignore inter-individual variability, leading to overdose. Recommendations reduce doses, depending on specific drugs.	-	-	**√**	-	-	-	**√**	**Reduce 30%**	-	-	-
5. Drug-drug Interactions: Risk of opoid overdose increased with certain drugs											
Sedative-hypnotics: Avoid, limit, taper sedative-hypnotics due to risk of mortality, excessive sedation, and motor vehicle accidents. Exceptions for seizures, spasticity, etc.	-	-	-	-	-	**√**	-	Indic-ated in some	-	-	-
Pharmacokinetic Interactions: List drugs affecting metabolism of selected opioids					**Meth-adone**	**Tram-adol**					**Meth-adone**
Metoclopramide and long-acting oral opioids: Faster absorption leads to overdose	-	-	-	-	**√**	-	-	-	-	-	-

6. Drug-disease Interactions: Risk of opioid overdose increased in selected populations											
Sleep Apnea, Sleep Disorders, Chronic Obstructive Pulmonary Disease	-	-	-	-	-	**√**	-	-	-	-	-
Renal Impairment: Any opioid except Hydromorphone	-	-	-	-	-	**√**	-	-	-	-	-
Cognitive Disorders, especially among people who live alone	-	-	-	-	-	**√**	-	-	-	-	-
Pre-existing Substance Abuse Disorders	-	-	**√**	-	-	-	-	-	-	-	-
Psychiatric Disorders: Depression, borderline personality disorder	-	-	**√**	-	-	-	-	-	-	-	-
Reducing the Risk of Substance Abuse											
7. Standardized Risk Assessment Instruments											
Recommend Use	**√**	-	**√**	**√**	**√**	**√**	-	**√**	**√**	**√**	**√**
List Tools for Use	-	-	**√**	-	-	**√**	-	**√**	-	-	**√**
8. Written Treatment Agreements											
Recommends Use	**√**	-	**Consi-der**	-	-	**√**	-	**√**	**√**	**√**	**√**
List Tools for Use	**√**		**√**								
9. Urine Drug Testing											
Recommends Use	**√**	-	**√**	-	-	**√**	-	**√**	**√**	**√**	**√**

- = not addressed by guideline